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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,247	07/01/2005	Mujun Zhao	SPT-0001	6598

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ART UNIT	**PAPER NUMBER**
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,247	ZHAO ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-5,8,9 and 11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/1/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of group III, now claims 6, 8, and 10, directed to a pharmaceutical composition comprising an antagonist of hLRTM4 gene transcript, wherein the antagonist is an antisense polynucleotide, and a pharmaceutically acceptable vesicle, diluent or carrier, in the reply filed on 6/15/07 is acknowledged.

Applicant argues that the special technical feature of the instant invention is the discovery of hLRTM4 and its roles in liver regeneration and GI cancers, as well as the ability of hLRTM4 to prevent and treat liver injuries, while antagonists of hLRTM4 can be used to treat liver and stomach cancers. The special technical feature of claim 1 is directed to a pharmaceutical composition comprising at least one selected from the group consisting of human liver regeneration associated protein hLRTM4, a polynucleotide comprising the hLRTM4 gene and a polynucleotide comprising a degenerate sequence of the hLRTM4 gene.

37 CFR 1.475(b) states:

"An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn **only** to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

37 CFR 1.475(c) states:

"If an application contains claims to more or less than one of the combination of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present."

37 CFR 1.475(d) also states:

"If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and 1.476(c)."

37 CFR 1.475(e) further states:

"The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternative within a single claim."

The claims are directed to more than one of the categories above. Specifically, the claims are directed to a pharmaceutical composition comprising at least one selected from the group consisting of human liver regeneration associated protein hLRTM4, a polynucleotide comprising the hLRTM4 gene and a polynucleotide comprising a degenerate sequence of the hLRTM4 gene (see claim 1); as well as to a method comprising administering the composition (see claim 4); as well as to a different pharmaceutical composition comprising an antagonist of hLRTM4 protein, gene or gene transcript (see claim 6); as well as to a method of administering the composition (see claim 9). Additionally, the claims recite multiple types of antagonists, which do not have unity of invention, as explained in the office action mailed on 4/17/07. Since the claims are directed to more than one of the combinations listed above, the instant claims do not have unity of invention as defined by 1.475(b).

Applicant asserts that the Administrative Instructions, Annex B, illustrates that the method for determining unity of invention under PCT Rule 13.2 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same application:

(i) in addition to an independent claim for a given product, an independent claim for a process specifically adapted for the manufacture of said product, and an independent claim for a use of said product...

Applicant asserts that all amended claims are directed to products or compositions and the uses of these products or compositions. However, as explained above, the instant claims do not meet the criteria because the claims are directed to multiple products and processes, rather than one product, a process for manufacture of that product, and a claim for use of that product.

Furthermore, there is no special technical feature as the pharmaceutical composition of claim 6 is not novel, as explained in the rejections under 35 USC 102(b), below. Therefore, there is no unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-5, 8, 9, and 11-15, as well as the subject matter that is not directed to the elected invention (antisense polynucleotide for the hLRTM4 gene transcript) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/15/07.

Newly added claim 11 is withdrawn as being drawn to a nonelected invention because claim 11 recites that the antagonist is a small interfering RNA and therefore belongs with group IV.

Newly added claims 12-15 are withdrawn as being drawn to a nonelected invention because claims 12-15 are directed to an isolated hLRTM4 protein or fragment

thereof, wherein hLRTM4 protein has a sequence of SEQ ID NO: 2; and to an isolated polynucleotide encoding the protein, wherein the isolated polynucleotide has a sequence of SEQ ID NO: 1; and to the isolated polynucleotide in an expression vector, and therefore belongs with group I.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/1/05 has been considered by the examiner. However, only the abstract could be considered in CN-1367179-A and WO-2004/060914-A1 because applicant has not provided a translation of the foreign documents.

Specification

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If

the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference

was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. It is noted that a translation of said papers has not been made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 7 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Instant claim 10 recites, "The composition of claim 7, wherein the antagonist is the antisense polynucleotide having a length of 15-625 nucleotides." The instant specification does not disclose antisense polynucleotides having a length of 15-625 nucleotides.

The instant specification discloses an antisense expression plasmid of nucleotides 16-625 of SEQ ID NO: 1, wherein SEQ ID NO: 1 is the coding region of the hLRTM4 gene (see example 6, pages 13 and 14 of the instant specification). The antisense sequence is the antisense of SEQ ID NO: 1 from nucleotides 16 to 625 and is therefore 610 nucleotides in length. This is not support for a size range of 15-625 nucleotides, but rather an antisense polynucleotide 610 nucleotides in length that is the antisense of nucleotides 16 to 625 of SEQ ID NO: 1.

Based on this example, the instant specification supports an antisense polynucleotide sequence that would target a gene transcript. However, the instant specification does not support the instant limitation wherein the antisense polynucleotide has a length of 15-625 nucleotides.

Additionally, the instant specification discloses that "this invention provides a pharmaceutical composition, which comprises a safe and effective amount of antagonists of hLRTM4 protein, wherein the antagonists are selected from the group consisting of: (i) **an antisense polynucleotide to hLRTM4 , wherein the polynucleotide has the antisense nucleotide sequence as shown in SEQ ID NO : 1 and has a length of 15-625bp**, and/or (ii) a specific antibody against hLRTM4, as well as a pharmaceutically acceptable vehicle, diluent or carrier." (see page 2 of the instant

specification). Therefore, the instant specification discloses the antisense polynucleotide disclosed in example 6, as explained above, and antisense polynucleotides that have the antisense nucleotide sequence as shown in SEQ ID NO: 1 and have a length of 15-625bp, as disclosed on page 2. Although the instant specification at page 2 refers to antisense polynucleotides that have SEQ ID NO: 1 and have a length of 15-625bp, these are not antisense polynucleotides to the hLRTM4 gene transcript, but are rather sense to hLRTM4 because they must have the sequence as shown in SEQ ID NO: 1, which is the coding region of the hLRTM4 gene (as disclosed on page 10 of the instant specification).

Therefore, the claim limitation "wherein the antagonist is the antisense polynucleotide having a length of 15-625 nucleotides" that was first introduced into the claims filed on 6/15/07 constitutes new matter. There is no support for this claim limitation in the claimed priority documents. Therefore, the effective filing date of instant claim 10 is considered, for purposes of prior art, to be 7/1/05, which is the filing date of the instant application.

A review of the specification does not reveal support for where the instant claim amendment is found. Should applicant disagree, applicants are encouraged to point out with particularity by page and line number where such support might exist.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Monia et al. (US 6,316,259 B1).

The instant claims are directed to a pharmaceutical composition comprising an antagonist of an HLRTM4 gene or gene transcript, wherein the hLRTM4 gene has a sequence of SEQ ID NO: 1 and a pharmaceutically acceptable vehicle, diluent, or carrier, wherein the antagonist is an antisense polynucleotide for the hLRTM4 gene transcript having a length of 15-625 nucleotides.

It is noted that the only structural limitation of the instant antisense polynucleotide to be an antagonist for the hLRTM4 gene transcript is having a length of 15-625 nucleotides. The instant claims do not require any specific function or level of complementarity to the target sequence.

Monia et al. teach an antisense oligomer 20 nucleotides in length wherein nucleotide 4-10 are 100% complementary to nucleotides 606-612 of instant SEQ ID NO: 1 (see SEQ ID NO: 87 in column 89 of Monia et al.) Furthermore, Monia et al. teaches a composition comprising the antisense compound and a pharmaceutically acceptable carrier or diluent (see claims 10 and 22). Although Monia et al. does not teach the antisense oligomer as being "for the hLRTM4 gene transcript" and an antagonist of hLRTM4 gene transcript, as instantly recited, the antisense oligomer of Monia et al. meets all of the structural limitations of the instant claims and therefore meets the criteria of being "for the hLRTM4 gene transcript" and an antagonist thereof. As stated

in the MPEP (see MPEP 2112), something that is old does not become patentable upon the discovery of a new property.

Therefore, the instant invention is anticipated by Monia et al.

Claims 6, 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Monia et al. (US 5,962,673).

The instant claims are directed to a pharmaceutical composition comprising an antagonist of an HLRTM4 gene or gene transcript, wherein the hLRTM4 gene has a sequence of SEQ ID NO: 1 and a pharmaceutically acceptable vehicle, diluent, or carrier, wherein the antagonist is an antisense polynucleotide for the hLRTM4 gene transcript having a length of 15-625 nucleotides.

It is noted that the only structural limitation of the instant antisense polynucleotide to be an antagonist for the hLRTM4 gene transcript is having a length of 15-625 nucleotides. The instant claims do not require any specific function or level of complementarity to the target sequence.

Monia et al. teach an antisense oligomer 18 nucleotides in length wherein nucleotide 3 and 5-18 are 100% complementary to nucleotides 458-471 and 473 of instant SEQ ID NO: 1 (see SEQ ID NO: 31 in column 55 of Monia et al. as well as SCORE Search Result File "20070803_131210_us-10-541-247-1.sl.rge", result #99) Furthermore, Monia et al. teaches a composition comprising the antisense compound and a pharmaceutically acceptable carrier or diluent (see column 12). Although Monia et al. does not teach the antisense oligomer as being "for the hLRTM4 gene transcript"

and an antagonist of hLRTM4 gene transcript, as instantly recited, the antisense oligomer of Monia et al. meets all of the structural limitations of the instant claims and therefore meets the criteria of being "for the hLRTM4 gene transcript" and an antagonist thereof. As stated in the MPEP (see MPEP 2112), something that is old does not become patentable upon the discovery of a new property.

Therefore, the instant invention is anticipated by Monia et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is (571) 272-0755. The examiner can normally be reached on Monday-Thursday 6:30 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amy H. Bowman/
Patent Examiner
Art Unit 1635